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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

PC 108102

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OCT 31 1981

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Memorandum

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

SUBJECT: PP#1E2515. Pirimiphos-methyl on Kiwifruit.
Evaluation of analytical methods and residue data.

FROM: John H. Onley, Ph.D., Chemist
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TO: Jay S. Ellenberger, Product Manager No. 12
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THRU: Charles L. Trichilo, Chief
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

ICI Americas Inc. originally proposed that tolerances be established in or on the imported raw agricultural commodity kiwifruit as follows:

"For the sum of residues of permethrin [(3-phenoxyphenyl)methyl cis:trans-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropane carboxylate] plus its metabolites cis:trans-3,(2,2-dichloroethenyl)-2,2-dimethylcyclopropane carboxylic acid and (3-phenoxyphenyl) methanol, calculated as permethrin, at 2 ppm.

"For the sum of residues of pirimiphos-methyl [O-(2-[diethylamino]-6-methyl-4-pyrimidinyl) O:O-dimethylphosphorothioate] plus its metabolites:

O-(2[ethylamino]-6-methyl-4-pyrimidinyl) O:O-dimethylphosphorothioate,
2-(diethylamino)-6-methyl-4 (3H) pyrimidinone,
2-(ethylamino)-6-methyl-4 (3H) pyrimidinone, and
2-amino-6-methyl-4 (3H) pyrimidinone

at 5 ppm.

Later, a request was made wherein we were asked to consider separately the proposed tolerances for permethrin and pirimiphos-methyl on kiwifruit [Telephone conversation between A. Hayward (HED) and R. Quick (HED)-7/6/81]; the proposed permethrin tolerance request in/on kiwifruit has been reviewed as a separate petition (see our 8/14/81 review of PP#1E2514).

Presently, no permanent pirimiphos-methyl tolerances have been established on any raw agricultural commodities.

Conclusions

1. The nature of the residue in plants and animals are adequately understood.

2. We do not have any information on the "Attack" formulation (47.5% pirimiphos-methyl and 2.5% permethrin) in our files; for this formulation, the petitioner needs to submit a statement of formulation that clearly defines the nature and amount of each ingredient, both active and inert. Also, a proposed label for the use of "Attack" on kiwifruit in New Zealand should be submitted.

3. The petitioner has anticipated that the U.S. Government will receive a letter from the government of New Zealand lending its support to this petition, confirming the agronomic value plus proposed use patterns for the product and indicating that registration in New Zealand will be forthcoming once adequate assurances have been obtained of the acceptability to major importing countries of residues in the treated crops. Such a letter has not yet been received. We will need such written assurance from the government of New Zealand confirming the proposed usage and the intent to register.

4a. A conclusion on the availability of an enforcement method for the parent compound, pirimiphos-methyl, for kiwifruit depends upon the outcome of the method trial that is presently in progress.

4b. For the present petition, we will not require a method trial on the methodology for the metabolites providing that there are no objections from TOX on the significance of these metabolites (see also Conclusion 5b below); for future usages, however, a method tryout for the metabolites will be needed.

5a. The proposed tolerance, if established, would be on the whole fruit (see 40 CFR 180.1(j)). The skin ordinarily is not eaten, but can be (United Fresh Fruits and Vegetables Association - March 1979 Publication). Well over 90% of the residue is on the peel of the kiwifruit.

5b. No residue data are submitted for the metabolites of pirimiphos-methyl. Residue data are submitted for the parent compound only. For purposes of this use on kiwifruit, we defer to TOX as to whether the four metabolites, 0-2-ethylamino-6-methyl-pyrimidin-4-yl 0,0-dimethyl; 2-diethylamino-6-methylpyrimidin-4-ol; 2-ethylamino-6-methylpyrimidin-4-ol; and 2-amino-6-methylpyrimidin-4-ol, need to be regulated in the terminal residue for toxicological purposes. RCB could recommend for the establishment of a 5 ppm tolerance on kiwifruit in terms of parent compound only, providing that the outcome of the pending method trial on the parent compound is successful. TOX should be advised, however, that RCB will require metabolites residue data for any future proposed use on other commodities. At that time, this kiwifruit tolerance, if established, will be revised to include the metabolites.

6. Normally, kiwifruit would not be fed to livestock or poultry. There would thus be no residue problems with regards to secondary residues in meat, milk, poultry and eggs.

7. An International Residue Limit Status Sheet is attached to this review. The proposed Codex limit of 2.0 ppm pirimiphos-methyl per se on kiwifruit is a Step 5 proposal, and is due to be sent to governments for comments this winter. Our residue calculations indicate that under the proposed use the terminal pirimiphos-methyl plus metabolites residues in/on kiwifruit should be covered by a 5.0 ppm tolerance.

Recommendations

We recommend that the proposed 5 ppm pirimiphos-methyl tolerance on kiwifruit not be established for the reasons given in Conclusions 2 and 3.

We ask the Product Manager to inform the petitioner of Conclusion 4b.

We defer to TOX on conclusion 5(b).

DETAILED CONSIDERATIONS

Manufacture and Formulation

For details of manufacturing process, see the RCB review of PP#9G2154 dated March 29, 1979.

Technical pirimiphos-methyl is a minimum of 90% pure. Impurities in the technical material include [redacted]

Section B of this petition refers to an emulsifiable concentrate formulation containing 47.5% pirimiphos-methyl and 2.5% permethrin. This formulation is intended to be known commercially as "Attach". No proposed label and confidential statement of formulation were submitted.

The permethrin proposed tolerance request in/on kiwifruit has been reviewed in a separate petition (see our 8/14/81 review of PP#1E2514).

With the advocacy of the aforementioned "Attack" formulation, we will need a statement of formulation that clearly defines the nature and amount of each ingredient, both active and inert, and a proposed label for the use of "Attack" on kiwifruit in New Zealand.

Proposed Use

To control greedy scale, Hemiberlesia rapax, dilute 1:1000 with water and spray at approximately 2,500 (0.0475% a.i.)/ha [equivalent to about 1 lb (pirimiphos-methyl) a.i./acre and spray volume of 267 gal/A].

Applications are required every four to six weeks. There is a minimum of 14 days between last application and harvest. Six or seven applications per season will be effective.

Nature of the Residue

Plants. A pirimiphos-methyl metabolism study has been submitted in the present petition. The treatment rates for the samples analyzed were 12.9 and 14.4 mg ^{14}C-pirimiphos-methyl/kg. Harvested fruit were spotted with the labeled material and placed outside under a plastic shelter. After 14 days in the sunlight, the total radioactive residue remaining on the whole fruit treated with pirimiphos-methyl at 12.9 mg/kg was 6.9 mg/kg pirimiphos-methyl equivalents of which 3.65 mg were pirimiphos-methyl. The total radioactive residue remaining on the fruit treated with pirimiphos-methyl at 14.4 mg/kg was 6.8 mg/kg pirimiphos-methyl equivalents of which 3.64 mg were pirimiphos-methyl. Over 90% of the residue remained on the peel.

The above results show that the terminal residues contained about 50% unidentified radioactivity. We would expect that a significant amount of this unidentified radioactivity could be present as the metabolites, O-2-ethylamino-6-methyl-pyrimidin-4-yl O,O-dimethyl; 2-diethylamino-6-methyl-pyrimidin-4-ol; 2-ethylamino-6-methyl-pyrimidin-4-ol; and 2-amino-6-methyl-pyrimidin-4-ol, since these metabolites were identified in the plant substrates of metabolism studies submitted previously (see N. Dodd review of PP#9G2200/FAP#9H5217). We will thus not request any further identification of the unidentified radioactive residues in the present study. We conclude that the nature of the residue in plants is adequately understood.

Animals. Metabolism studies in chickens, cows, dogs, goats, and rats were discussed fully in our reviews of PP#9G2154 (3/29/79 - R. Perfetti) and PP#9G2200/FAP#9H5217 (4/10/80 - N. Dodd).

We consider the nature of the residue in animals to be adequately understood.

Analytical Methods

Method I. This is a GLC procedure that can analyze plant and animal samples for the parent compound pirimiphos-methyl and one of its metabolites, O-2-ethylamino-6-methyl-pyrimidin-4-yl O,O-dimethyl phosphorothioate. Kiwifruit samples are extracted with 20% acetone in n-hexane by blending. The samples are washed with water, dried with anhydrous sodium sulfate and then analyzed by a gas chromatograph equipped with a flame photometric or thermionic detector. The procedure has built-in steps that permit the analyses of other commodities such as grains, animal tissues, milk, eggs, etc.

Individual recovery values for pirimiphos-methyl and O-2-ethylamino-6-methyl-pyrimidin-4-yl O,O-dimethyl phosphorothioate in kiwifruit were not submitted. The petitioner used a chemical efficiency of 67% in the calculations of the pirimiphos-methyl residue data submitted. The petitioner also states that recoveries in crop samples between the 0.1-5 ppm levels are usually in the range 90 + 10%. The limit of detection for pirimiphosmethyl in kiwifruit is about 0.05 ppm. We have submitted this method to our Method Trial Unit for validation. Our conclusion on the subject analytical methodology will depend upon the success of the method trial that is presently in progress.

Method II. The petitioner has also presented a procedure for the determination of residues of the hydroxypyrimidine metabolites, (I) 2-diethylamino-6-methyl-pyrimidin-4-ol; (II) 2-ethylamino-6-methylpyrimidin-4-ol; and (III) 2-amino-6-methylpyrimidin-4-ol; in kiwifruit.

A sample is extracted with methanol: 2M HCl (90:10) by blending. An aliquot is washed with hexane and them concentrated to dryness. The sample is dissolved in pH 7 phosphate buffer solution and cleaned up first on an Extrelut® column; it is cleaned up further on a Fractosil 200 column. Finally, the metabolites (sample residues) are derivitized with N,O-Bis-(trimethylsilyl)-trifluoroacetamide (BSTFA) and determined by gas liquid chromatography/mass spectrometry.

Individual recovery values for the above metabolites, I, II and III, were not submitted. The petitioner, in brief, states that at fortification levels of 0.1 to 1.0 ppm the recovery ranges for Metabolites I, II, and III on whole fruit were 80% + 3%, 87% + 7% and 79% + 3%, respectively. The limit of determination was given as 0.01 mg/kg for each metabolite.

For the present use on kiwifruit, RCB will not require EPA validation of the metabolites methodology providing that TOX can conclude that the proposed kiwifruit tolerance can be established in terms of parent compound only. However, the metabolites methodology must be validated by EPA before the establishment of any future tolerances.

Residue Data

Residue data on kiwifruit involved samples collected at 2 locations in New Zealand. These studies involved the combined usages of permethrin and pirimiphos-methyl. Permethrin residue data were reviewed in PP#1E2514. The present review is concerned with pirimiphos-methyl residues only.

In the present studies, kiwifruit crops received 3-7 (1 lb. a.i.) applications of Attack per acre per season. The data for the parent compound only are summarized below:

PHIs, days	Crop Parts	ppm Found
7	Whole	1.8-3.1
14	"	1.8-2.3
28	"	1.0
42-56	"	<0.06-1.1
70-85	"	<0.06-0.1
14	Skin	9-10
28	"	4
14	Pulp	<0.06
28	"	<0.06

A pirimiphos-methyl tolerance on kiwifruit would be established on a whole fruit basis [40 CFR 180l(j)]. The skin ordinarily is not eaten, but can be (United Fresh Fruits and Vegetable Association - March 1979 Publication). The above data indicate that whole kiwifruit receiving 3-7 applications could contain up to 2.3 ppm pirimiphos-methyl at harvest at the proposed minimum PHI of 14 days. The ^{14}C-metabolism study on kiwifruit indicated that about 50% of the terminal residues could be metabolites and/or conjugates after 14 days. No metabolite residue data were submitted in the present petition.

With regards to the present petition, we have considered the dietary intake of kiwifruit and thus defer to TOX as to whether the four metabolites, O-2-ethylamino-6-methylpyrimidin-4-yl O,O-dimethyl; 2-diethylamino-6-methylpyrimidin-4-ol; 2-ethylamino-6-methylpyrimidin-4-ol; and 2-amino-6-methylpyrimidin-4-ol, need to be regulated in the terminal residue for toxicological purposes. RCB could recommend for the establishment of a 5 ppm tolerance on kiwifruit in terms of parent compound only providing that the outcome of the pending method trial on the parent compound is successful. However, TOX should be advised that for any future proposed usages of pirimiphos-methyl on other commodities, we will require metabolites residue data and a successful EPA method trial involving the four aforementioned metabolites. At that time, this kiwifruit tolerance, if established, will be revised to include the metabolites. The inclusion of the above 4 metabolites in the tolerance regulations is consistent with our recommendations expressed at the June 1980 meeting (see our Memo of Conference July 2, 1980).

Meat, Milk, Poultry and Egg Residues

Normally, kiwifruit would not be fed to livestock and poultry. There would thus be no residue problems with regards to secondary residues in meat, milk, poultry and eggs.

Other Considerations

The petitioner has anticipated that the U.S. Government will receive a letter from the government of New Zealand lending its support to this petition, confirming the agronomic value plus proposed use patterns for the product, and indicating that registration in new Zealand will be forthcoming once adequate assurances have been obtained of the acceptability to major importing countries of residues in the treated crops. Such a letter has not yet been received. We will need such written assurance from the government of New Zealand confirming the proposed usage and the intent to register.

TS-769:RCB:J. Onley:gs:X77377:CM#2:RM810:10-31-81
cc: RF, Circ., Onley, Watts, FDA, TOX, EEB, EFB, PP#1E2515
RDI: Quick, 10-21-81: Schmitt, 10-21-81

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL Pirimiphos-methyl PETITION NO. 1E2515 Reviewer: J. Onley

CCPR NO. 86

Codex Status

/ / No Codex Proposal Step 6 or above

Proposed U.S. Tolerances

Residue (if Step 9): Combined residues of pirimiphos-methyl, its oxygen analog and N-desethylpirimiphos-methyl expressed as pirimiphos-methyl

Crop(s)	Limit (mg/kg)
Kiwifruit	2 1/

Residue: Pirimiphos-methyl

Crop(s)	Tol. (ppm)
Kiwifruit	5

CANADIAN LIMIT

Residue:

Crop	Limit (ppm)
None	

MEXICAN TOLERANCIA

Residue:

Crop	Tolerancia (ppm)
None	

Notes: 1/ This a Step 5 proposal, and is due to be sent to governments for comments this winter.

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Chemical:	**Pirimiphos-methyl (ANSI)**
PC Code:	**108102**
HED File Code	**11000 Chemistry Reviews**
Memo Date:	**10/31/81**
File ID:	**00000000**
Accession Number:	**412-03-0015**

HED Records Reference Center
09/23/2002